

Attorney Docket No.: DEX-0180  
Inventors: Roberto A. Macina  
Serial No.: 09/806,302  
Filing Date: July 19, 2001  
Page 4

#### REMARKS

Claims 1-5 are pending in the instant application. Claims 1-5 have been rejected. Claim 1 has been amended and claims 2 through 5 have been canceled. Support for the amendments is provided in the specification at pages 16-22 and particularly page 22. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### **I. Rejection of Claims 1, 3, 5-6 under 35 U.S.C. § 112, first paragraph**

Claims 1, 3 and 5 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Examiner suggests that there is both overexpression and underexpression in cancerous endometrial samples. Further, the Examiner suggests that there is no data supporting a relationship between mRNA levels or protein levels and diagnostic test endpoints of assessing cancer stage and monitoring cancer stage. In addition, the Examiner suggests that there is no data in the specification demonstrating correlation

Attorney Docket No.: DEX-0180  
Inventors: Roberto A. Macina  
Serial No.: 09/806,302  
Filing Date: July 19, 2001  
Page 5

between protein levels and gynecologic cancer.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have canceled claims 2 through 5 drawn to monitoring and staging cancers, thus mooting the Examiner's concerns regarding a lack of data showing a relationship between mRNA levels or protein levels and these diagnostic test endpoints.

Further, Applicants have amended claim 1 to be drawn to a method for detecting the presence of uterine or ovarian cancer. As taught at page 22 of the instant application, overexpression was observed in all uterine cancer samples examined and median expression in ovary cancer samples was 28.1 as compared to expression in normal ovary samples which was 0. Accordingly, this amendment renders moot the Examiner's concerns regarding variation in expression in endometrial cancer samples.

Applicants respectfully disagree with the Examiner's suggestion that the three cited references of Shantz and Pegg (Int. J. of Biochem. and Cell Biol. 1999 31:107-122), McClean and Hill (Eur. J. Cancer 1993 29A:2243-2248) and Fu et al. (EMBO Journal 1996 15:4392-4401) establish unpredictability of a correlation between steady state mRNA levels and steady state protein levels for cancer markers, while the reference of Lopez-

Attorney Docket No.: DEX-0180  
Inventors: Roberto A. Macina  
Serial No.: 09/806,302  
Filing Date: July 19, 2001  
Page 6

Guerrero et al. (Arkh Patol. 2003 65(1):50-5) provided by Applicants in the last response fails to demonstrate such a correlation. The three references cited by the Examiner report unique findings for a disparate group of proteins wherein mRNA expression did not correlate with protein expression. Applicants do not believe that these references are representative of what is believed by those skilled in the art.

Instead, teachings far more representative of the general understanding of those skilled in this art field can be found in references such Lopez-Guerrero et al. (Arkh Patol. 2003 65(1):50-5) submitted previously, and additional abstracts submitted herewith by Jaakola et al. (Clin Chem. 1995 41(2):177-9), el-Shirbiny et al. (Adv. Clin. Chem. 1994 31:99-133) and Straub et al. (Urology 2001 58(5):815-20) showing the correlation between mRNA expression and protein levels of a well known cancer marker, PSA.

MPEP § 2164.04 states:

a specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Attorney Docket No.: DEX-0180  
Inventors: Roberto A. Macina  
Serial No.: 09/806,302  
Filing Date: July 19, 2001  
Page 7

The instant specification provides detailed teachings of diagnostic methods for ovarian and uterine cancer at pages 8 through 10. Detailed assay techniques for detecting an ESBPIII comprising a polynucleotide sequence of SEQ ID NO:1 or a protein encoded thereby in accordance with claim 1 are set forth in the specification at pages 11 through 14. In addition, detectable elevated levels of ESBPIII in ovarian and uterine cancer are demonstrated by the data presented in the specification at pages 16-22. Thus, the instant specification clearly teaches one of skill how to make and use the instant claimed invention.

Further, art much more relevant to the instant claimed invention than that cited by the Examiner is supportive of the fact that polynucleotide levels of cancer markers are expected to correlate with polypeptide levels. Accordingly, there is no reasonable basis to question the teachings of the instant specification.

Thus, the instant specification and claims meet the enablement requirements of 35 U.S.C. § 112, first paragraph. Withdrawal of this rejection is therefore respectfully requested in light of the above remarks and amendments to the claims.

Attorney Docket No.: DEX-0180  
Inventors: Roberto A. Macina  
Serial No.: 09/806,302  
Filing Date: July 19, 2001  
Page 8

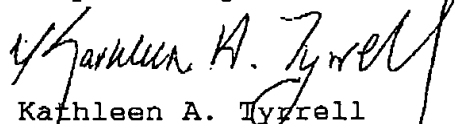
## II. Rejection of Claims 2 and 4 under 35 U.S.C. § 102(e)

Claims 2 and 4 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Lehrer. It is respectfully pointed out, however, that claims 2 and 4 have been canceled, thus mooted this rejection. Withdrawal of this rejection under 35 U.S.C. § 102(e) is therefore respectfully requested.

## III. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

  
Kathleen A. Tyrrell  
Registration No. 38,350

Date: February 5, 2004

LICATA & TYRRELL P.C.  
66 E. Main Street  
Marlton, New Jersey 08053

(856) 810-1515